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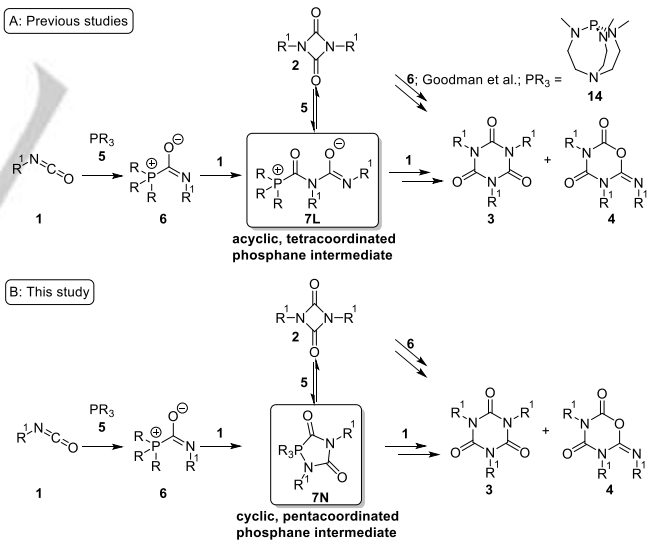
Mechanistic Analysis and Characterization of Intermediates in the Phosphane-Catalyzed Oligomerization of Isocyanates

Julian Helberg,[a] Yohei OE,[b] Hendrik Zipse*[a]

Abstract: The mechanism of the oligomerization of aliphatic isocyanates catalyzed by trialkylphosphanes has been studied through low temperature ^{31}P and ^{15}N NMR spectroscopy combined with computational chemistry. A revised mechanism is proposed that contains several (spiro)cyclic pentacoordinate phosphorous intermediates. Previously reported spectroscopic data of a transient intermediate has been reevaluated and assigned to a cyclic intermediate containing a P-N bond by experiments with ^{15}N-labeled isocyanate. ^{13}C, ^{15}N and ^{31}P NMR shifts that support this assignment have been calculated using quantum chemical methods.

The oligomerization of aliphatic isocyanates **1** using Lewis base catalysts is an important industrial process for the synthesis of building blocks for highly durable polyurethane (PU) coatings.[1] The use of oligomers provides a higher degree of safety during the polymerization process due to significantly lower vapor pressures and provides the basis for tuning polymer properties.[2] Addition of (aliphatic) isocyanurates **3** often enhances the physical properties of polymers, for example in the production of flame retardant materials used for the lamination of electrical devices.[3] Depending on the Lewis base catalyst and the reaction conditions, the oligomerization of isocyanates generates variable amounts of uretdiones **2**, isocyanurates **3**, iminooxadiazinediones **4**, and higher oligomers (Scheme 1A). In the case of trialkylphosphane-catalyzed oligomerizations of aliphatic isocyanates, the reaction is believed to be initiated through attack of phosphane **5** at the central carbon atom of isocyanate **1** and formation of zwitterion **6** as a first transient intermediate. Subsequent reaction of **6** with a second equivalent of isocyanate then generates acyclic, tetracoordinated phosphane intermediate **7L**, whose detection by low temperature ^{31}P and ^{13}C NMR spectroscopy was reported by Horvath et al. for the oligomerization of aliphatic isocyanate **1** catalyzed by *tri*-alkylphosphane **5**.[2a,4] The reaction then either proceeds through elimination of catalyst **5** and (reversible) formation of uretdione **2**, or addition of a third isocyanate monomer and elimination of catalyst **5** to form isocyanurate **3** or iminooxadiazinedione **4**. Based on a computational study on the azaphosphatrane **14**-catalyzed oligomerization of isocyanates, Goodman et al. proposed another pathway to the trimers **3** and **4** by reaction of monoadduct **6** with uretdione **2**. They also suggested stabilization of intermediate **7** as a five membered ring in which O coordinates to P (labeled **7O** in this study).[5]

The ^{31}P NMR signal at −54.0 ppm assigned by Horvath et al. to the acyclic, tetracoordinated phosphane intermediate **7L** does neither remotely fit the chemical shift (>0 ppm) usually associated with tetracoordinated phosphorus,[2a,6] nor the one published for monoadduct **6** of azaphosphatrane **14** and phenyl isocyanate (+29.46 ppm) by Verkade.[7] This prompted us to reinvestigate the mechanism proposed for the phosphane-catalyzed oligomerization of alkyl isocyanates **1**, using a combination of computational NMR shift predictions and experimental NMR measurements employing ^{15}N labeled isocyanate. Herein, we show a quantitative assignment for the signals reported previously and in consequence, propose a new mechanism including key intermediate **7N** for the phosphane-catalyzed oligomerization of aliphatic isocyanates (Scheme 1B).



Scheme 1. Simplified mechanism showing key intermediates in the phosphane-catalyzed oligomerization of aliphatic isocyanates **1** in previous studies (A) and in the current study (B).

Initially, we reproduced the kinetic measurements and low-temperature NMR experiments published by Horvath et al. and were able to confirm these results while using a different analytical method for the kinetics.[2a] Figure 1 shows the time-resolved oligomerization of *n*-hexyl isocyanate **1a** measured by ^{1}H NMR which indicates that the initial formation of dimer **2a** and

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subsequent formation of trimers **3a** and **4a** proceeds in a tightly coupled fashion.

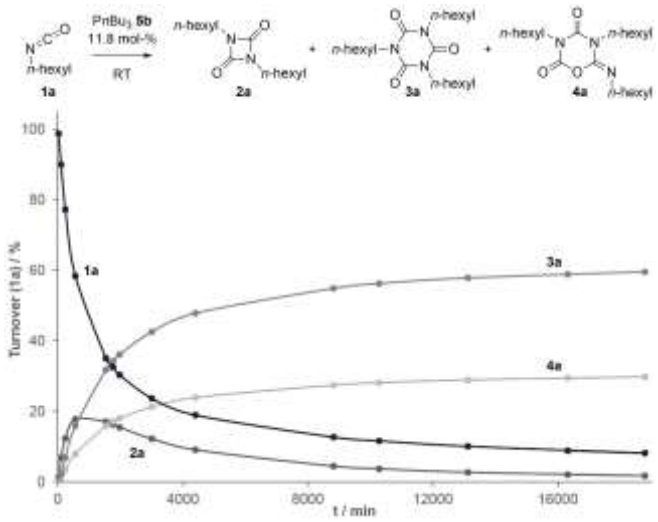


Figure 1. Time-resolved oligomerization of **1a** observed by ^{1}H NMR spectroscopy.

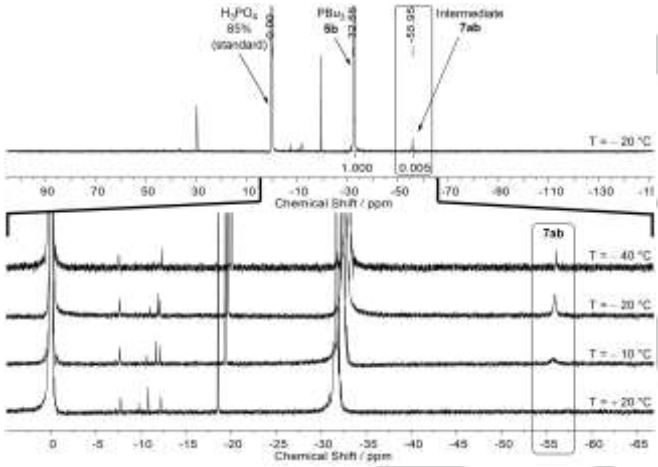
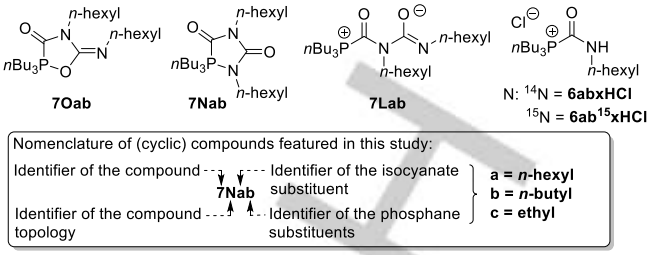


Figure 2. ^{31}P{^{1}H} NMR spectra of the reaction of **1a** and **5b** (50 mol-%): top: at −20 °C; bottom: spectra at different temperatures.

Low-temperature NMR measurements were performed under neat conditions on oligomerization reactions of isocyanate **1a** catalyzed by 50 mol-% **5b**. Figure 2 (top) shows the proton decoupled ^{31}P NMR spectrum at −20 °C with integrals for two species: catalyst **5b** and intermediate **7ab**. Bis-adduct **7ab** appears as a temperature-dependent signal at −55.7 ±0.4 ppm with an integral of approx. 0.5% of free phosphane **5b** that broadens and shifts with increasing temperature (bottom). Since we suspected the signal of intermediate **7ab** to represent one of the cyclic, pentacoordinate intermediates **7Nab** or **7Oab** rather than acyclic, tetracoordinated **7Lab** (Scheme 2), the low temperature NMR measurements were repeated with ^{15}N labeled *n*-hexyl isocyanate **1a^{15}**.



Scheme 2. Conceivable structures for intermediate **7ab** and H^{+}-trapped model compound **6abxHCl**.

This allows the differentiation of the possible intermediates shown in Scheme 2 based on their ^{31}P/^{15}N couplings and ^{15}N chemical shifts. **1a^{15}** was obtained in three steps starting from heptanoic anhydride and $^{15}NH_4Cl$ (see SI). In order to obtain a stable reference compound structurally related to the potential intermediate, the H^{+}-trapped phosphonium **6ab×HCl** and its ^{15}N-labeled analogue **6ab^{15}×HCl** were synthesized *in situ* by mixing of equimolar amounts of isocyanate **1a** and tri-*n*-butylphosphonium chloride **16b** (see SI). This resulted in next-to-quantitative formation of **6ab×HCl** as verified by ^{1}H, ^{31}P, ^{13}C NMR spectroscopy and high resolution mass spectroscopy. The ^{31}P NMR spectrum of compound **6ab×HCl** shows a singlet at a typical "phosphonium" chemical shift of +29.6 ppm that turns into a doublet (J = 28.4 Hz) in the case of the ^{15}N-labled **6ab^{15}×HCl**. The ^{15}N NMR spectrum of this compound shows a doublet of doublets at −236.54 ppm, formed by ^{1}H/^{15}N coupling (J = 90.7 Hz) and ^{31}P/^{15}N coupling (J = 28.4 Hz).

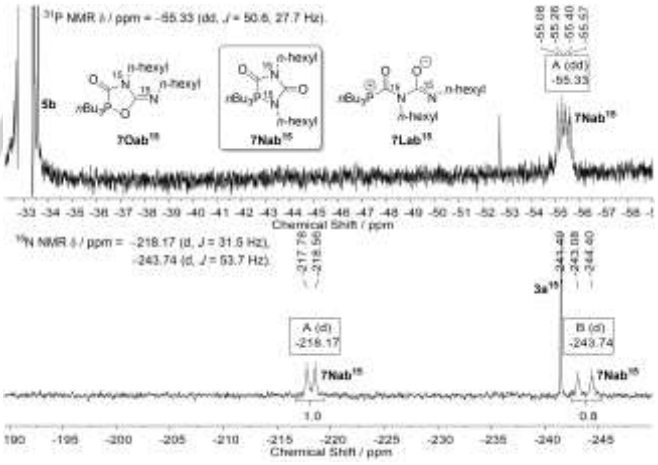


Figure 3. NMR spectra of the reaction of **1a^{15}** and **5b** (50 mol-%) at −40 °C: ^{31}P{^{1}H} spectrum showing intermediate **7Nab^{15}** to form a doublet of doublets (top) and ^{15}N spectrum with the corresponding doublets (bottom).

Repeating the earlier NMR measurements at −40 °C using **1a^{15}** and 50 mol-% **5b** yields a proton decoupled ^{31}P spectrum where the intermediate signal appears as a well-defined doublet of doublets with coupling constants of J = 50.6 Hz and J = 27.7 Hz (Fig. 3). ^{15}N NMR shows the corresponding doublets at −218.2 ppm (J = 31.5 Hz) and −243.7 ppm (J = 53.6 Hz).

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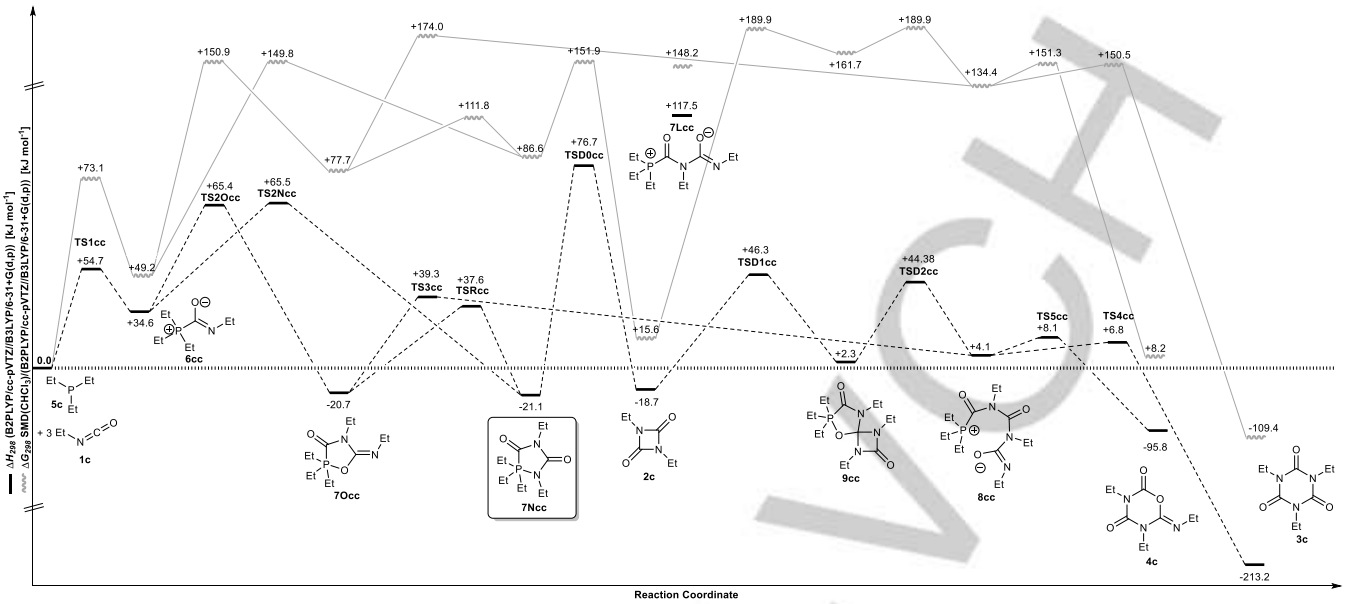
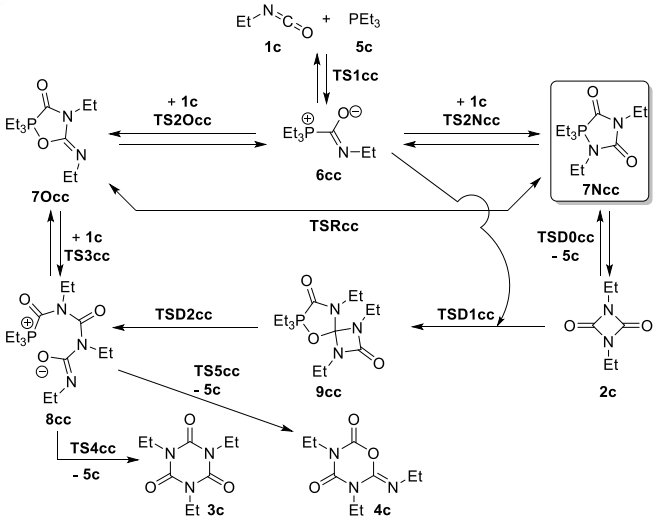


Figure 4. Potential energy surface of the oligomerization of ethyl isocyanate **1c** catalyzed by triethylphosphane **5c** [in kJmol^{-1}].

The minor deviation in the coupling constants results most likely from the ^{15}N NMR being measured in a proton coupled fashion. This is required because the doublet at −243.7 ppm does not appear in proton decoupled ^{15}N NMR, presumably due to Nuclear Overhauser Effects. The doublet at -218.2 ppm gives a coupling constant of J = 27.5 Hz in the proton decoupled measurements in complete agreement with the ^{31}P NMR results (see SI).

Since the ^{15}N atoms show coupling only to the ^{31}P atom, assignment of both signals is possible based on the spectroscopic data for **6ab^{15}×HCl**. Comparison of the coupling constants in ^{15}N NMR spectroscopy clearly shows, that the doublet generated by intermediate **7Nab** at −218.17 ppm (J = 27.5-31.5 Hz) represents the nitrogen atom next to the P-bound carbonyl group. Since the other ^{15}N doublet at −243.74 ppm (J = 53.6 Hz) shows a much larger coupling constant and therefore stronger coupling, we see this as evidence of the second ^{15}N atom being closer to the phosphorous atom in the detected intermediate. This strongly supports assignment of cyclic, pentacoordinate phosphane **7Nab**[15] as the observed intermediate as highlighted in Figure 3. The preference of phosphorous atoms to form cycles by bonding to isocyanate nitrogen atoms rather than the oxygen atoms is not unprecedented. Neutral cyclic monoalkyl phosphanes structurally similar to **7Nab** were generated by condensation of phospholenes and isocyanates, and more recently Grützmacher et al. reported several cyclic, anionic P-N bond containing species found in the cyclo-oligomerization of isocyanates by "P^{-}" anions.[8]

Having obtained experimental evidence that the observed intermediate is cyclic, pentacoordinate phosphane **7Nab**, we decided to use computational chemistry to further elucidate the reaction mechanism. We found that consistent results were obtained at the B2PLYP/cc-pVTZ//B3LYP/6-31+G(d,p) level of theory and used a SMD($CHCl_3$) solvation model to simulate the rather polar conditions in the oligomerization mixture.[9] Figure 4 shows the potential energy surface (gas phase ΔH_{298} and solution phase ΔG_{298}) for the triethylphosphane-(**5c**)-catalyzed oligomerization of ethyl isocyanate **1c**. In the following, the discussion focusses on the gas-phase enthalpy values (ΔH_{298}). It is noteworthy, that acyclic intermediate **7Lcc** is much less stable than the corresponding cyclic isomers **7Occ** and **7Ncc**, which are both located significantly lower in energy. Of these two cyclic bis-adducts, **7Ncc** is slightly preferred.



Scheme 3. Proposed reaction mechanism of the (alkyl) phosphane – catalyzed oligomerization of alkyl isocyanates formulated for all-ethyl substituents in analogy to the computational study.

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While initial formation of the cyclic intermediates **7Occ** and **7Ncc** is possible through reaction of monoadduct **6cc** with another monomer **1c**, interconversion is also possible via transition state **TSRcc** located +58.8 kJmol^{-1} above **7Ncc**. Uretdione **2c** is exclusively formed from cyclic intermediate **7Ncc** through transition state **TSD0cc**. Dimer **2c** is then able to react with monoadduct **6cc** forming previously unreported *spiro*-intermediate **9cc**, which is conceptually similar to the *spiro*-tetramers formed by reductive oligomerization in the presence of silanes reported by Süss-Fink.[10] Acyclic, trimeric intermediate **8cc** is either formed by interconversion of **9cc** through transition state **TSD2cc** or by addition of one molecule of **1c** to cyclic adduct **7Occ** through transition state **TS3cc**. Trimers **3c** and **4c** are finally obtained from **8cc** via the low-lying transition states **TS5cc** and **TS4cc**. Based on both the experimental and computational results, we propose the revised reaction mechanism shown in Scheme 3.

For all intermediates found in the revised mechanism, ^{13}C, ^{15}N, and ^{31}P NMR chemical shifts were predicted at the B3LYP/IGLO-III//B3LYP/6-31+G(d,p) level of theory (see SI). The methodology used combines theoretically calculated shieldings for the ethyl-substituted systems shown in Figure 4 with a system of increments for the influence of longer alkyl chain substituents. The predicted ^{31}P chemical shifts perfectly fit our assignment of cyclic, pentacoordinate intermediate **7Nab** to the signals reported by Horvath and Richter (theor. predicted -55.2 ppm, exp. found -55.6 ppm here and -55.0 ppm in ref. 2).[2a] In addition, the predicted ^{31}P chemical shift for acyclic intermediate **7Lab** of +29.3 ppm is that for a "typical" phosphonium species. In case of ^{15}N NMR spectroscopy, the predicted signals vary more from the measured ones, probably because of the partially anionic character of the nitrogen atoms in the intermediates that was not reflected in our set of reference compounds. Still, **7Nab** is the only intermediate whose predicted NMR shifts fit for all three measured nuclei in complete agreement with all other results.

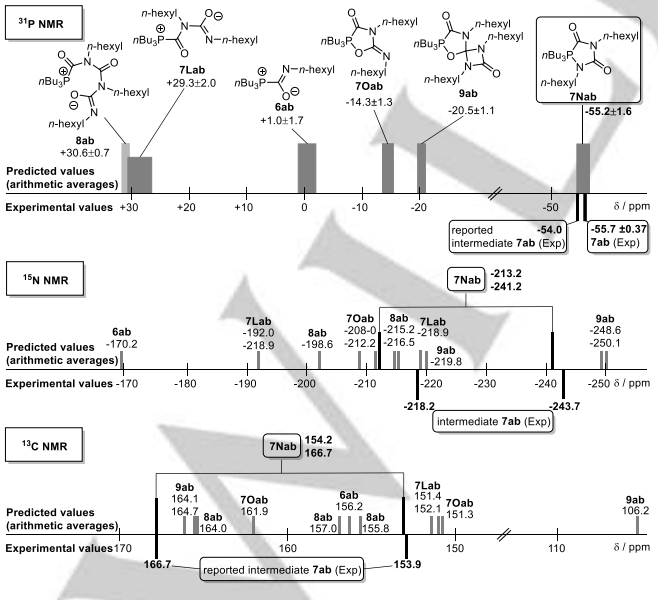

Figure 5. Comparison of predicted and experimentally obtained ^{31}P, ^{15}N and ^{13}C NMR shifts.

In conclusion, we provide here a comprehensive study on the phosphane-catalyzed oligomerization of aliphatic isocyanates, which includes the validation of earlier ^{31}P NMR and kinetic measurements,[2a] and the combined experimental/theoretical analysis of ^{15}N and ^{31}P NMR spectral data in reactions of ^{15}N-labeled isocyanates. Calculation of the potential energy surface leads us to a revised reaction mechanism featuring previously unknown spiro intermediate **9** formed from uretdione **2**. Cyclic intermediate **7N** is responsible for the signals visible at low temperature NMR measurements as shown by the prediction of ^{31}P, ^{15}N and ^{13}C chemical shifts. Further evidence was obtained from the ^{31}P-^{15}N couplings and the multiplicities found for signals in low temperature NMR measurements. The new mechanism provides the basis for a better understanding of an important industrial process and its possible improvement through the development of new catalyst systems. This study also shows the potential of the employed methodology to solve further unanswered questions of isocyanate activation by organocatalysts.[11]

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Keywords: Computational chemistry, isotopic labelling, Lewis base organocatalysis, NMR spectroscopy, reaction mechanisms

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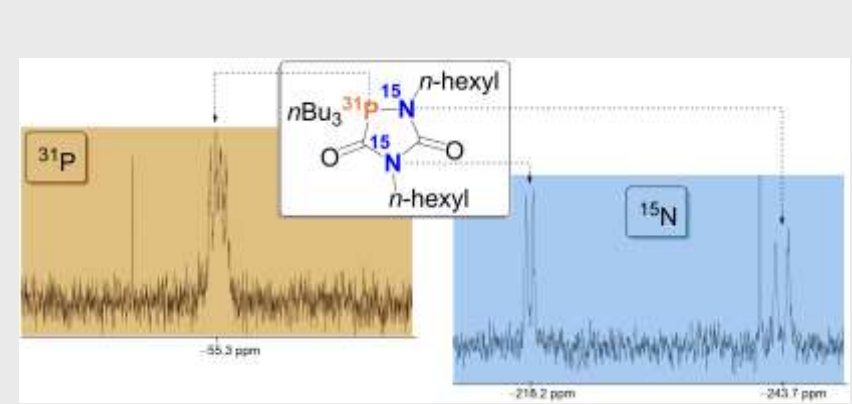

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